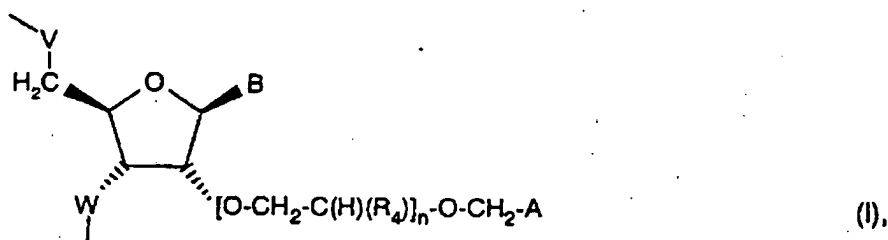


Amendments to the Claims

This Listing of the Claims will replace all prior versions, and listings, of claims in the application.

Listing of the Claims:

1. (Currently Amended) An oligonucleotide derivative comprising at least one nucleoside building block of the formula (I)



in which

A is a radical of the formula $-C(H)(R_3)-N(R_1)(R_2)$, in which

R_1 and R_2 are, independently of each other,

H,

C_1-C_{10} alkyl,

a radical of the formula II



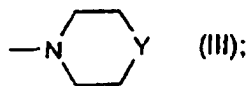
in which each X is, in each case independently of each other, O or $N(R_6)$, R_5 and R_6 are, in each case independently of each other, H, C_1-C_{10} alkyl, amino- C_2-C_{10} alkyl, N-mono- C_1-C_{10} alkylamino- C_2-C_{10} alkyl or N,N-di- C_1-C_{10} alkylamino- C_2-C_{10} alkyl, and m is an integer from 1 up to and including 3,

amino- C_3-C_{10} alkyl,

N-mono- C_1-C_{10} alkylamino- C_3-C_{10} alkyl, or

N,N-di- C_1-C_{10} alkylamino- C_3-C_{10} alkyl; or in which

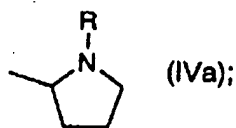
$-N(R_1)(R_2)$ are together a radical of the formula (III),



in which Y is O, S, SO, SO₂ or $N(R_7)$, and R_7 is H or $-CH_3$;

R_3 is H, $-CH_3$, $-CH_2CH_3$, $-CH_2OH$ or $-CH_2O-C_1-C_4$ alkyl; or

A is a radical of the formula (IVa) or (IVb)



in which R, independently, has the meaning of R_1 , or R_2 , and U is O or CH_2 ;

R_4 is H, $-\text{CH}_3$, $-\text{CH}_2\text{CH}_3$, $-\text{CH}_2\text{OH}$ or $-\text{CH}_2\text{O}-\text{C}_1-\text{C}_4\text{alkyl}$;

n is 0, 1 or 2;

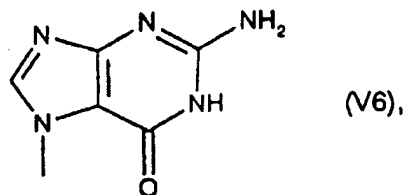
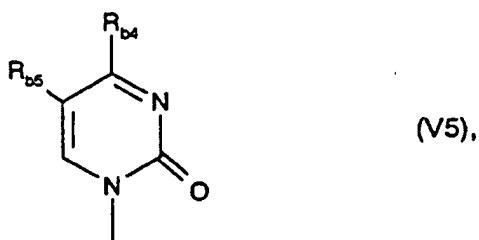
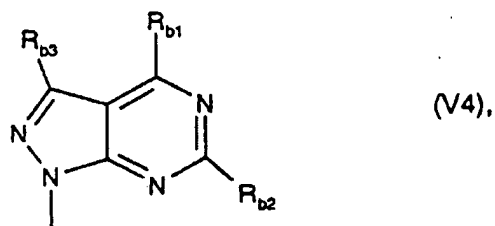
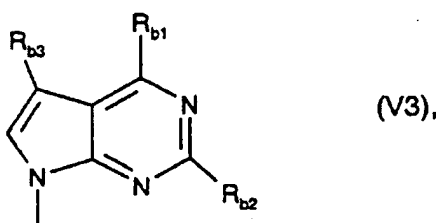
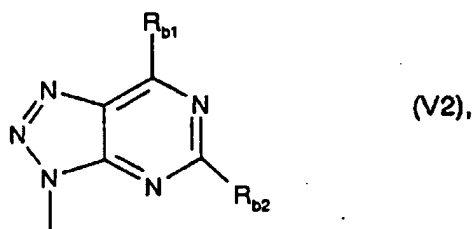
B is the radical of a nucleic acid base; and

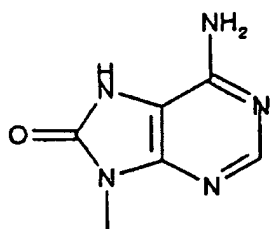
V and W are, independently of each other, the same or different radicals of an internucleosidic bridging group or are a terminal radical;

and a salt thereof;

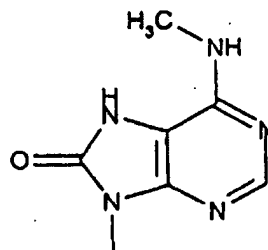
where those compounds are excepted in which, in the radical A, two heteroatoms are linked to the same carbon atom atom,

wherein B is a radical of any of the formulas (V2) to (V14):

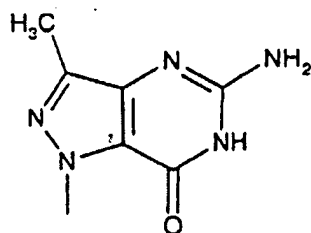




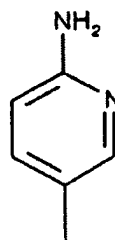
(V7),



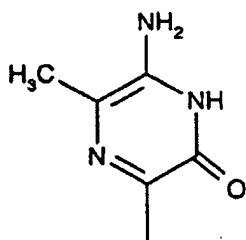
(V8),



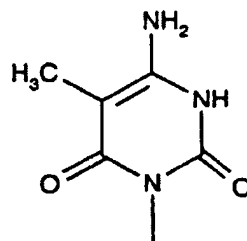
(V9),



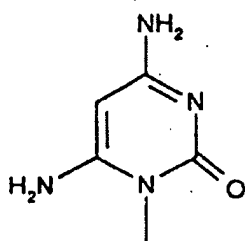
(V10),



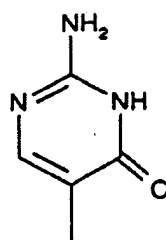
(V11),



(V12),



(V13),



(V14)

in which

R_{b1} is $-NH_2$, $-SH$ or $-OH$;

R_{b2} is H , $-NH_2$ or $-OH$; and

R_{b3} is H , Br , I , $-CN$, $-C\equiv C-CH_3$, $-C(O)NH_2$ or $-CH_3$;

R_{b4} is $-NH_2$ or $-OH$; and

R_{b5} is H , F , Br , I , $-CN$, $-C\equiv C-CH_3$, $-C(O)NH_2$ or $-CH_3$.

2. (Previously Presented) The oligonucleotide derivative according to claim 1, in which A is a radical of the formula $-C(H)(R_3)-N(R_1)(R_2)$, in which

R_1 and R_2 are, independently of each other, H , C_1 - C_5 alkyl, amino- C_2 - C_5 alkyl, N-mono- C_1 - C_3 alkylamino- C_2 - C_5 alkyl, N,N-di- C_1 - C_3 alkylamino- C_2 - C_5 alkyl or a radical of the formula II



in which X is O or N(R₆), R₅ and R₆ are, independently of each other, H, C₁-C₃alkyl, amino-C₂-C₃alkyl, N-mono-C₁-C₃alkylamino-C₂-C₅alkyl or N,N-di-C₁-C₃alkylamino-C₂-C₅-alkyl, and m is 1.

3. (Previously Presented) The oligonucleotide derivative according to claim 2, in which R₁ and R₂ are, independently of each other, H, methyl, ethyl, aminoethyl, aminopropyl, N-monomethylaminoethyl, N-monomethylaminopropyl, N-monoethylaminoethyl, N-monoethylaminopropyl, N,N-dimethylaminoethyl, N,N-dimethylaminopropyl, N,N-diethylaminoethyl, N,N-diethylaminopropyl, or a radical of the formula II



in which X is O or N(R₆), R₅ and R₆ are, independently of each other, H, methyl, ethyl or propyl, and m is 1.

4. (Previously Presented) The oligonucleotide derivative according to claim 3, in which R₁ and R₂ are, independently of each other, H, methyl, ethyl, aminoethyl, N-monomethylaminoethyl, N-monoethylaminoethyl, N,N-dimethylaminoethyl or N,N-diethylaminoethyl.

5. (Previously Presented) The oligonucleotide derivative according to claim 4, in which R₁ and R₂ are, independently of each other, H, methyl or ethyl.

6. (Previously Presented) The oligonucleotide derivative according to claim 5, in which R₁ and R₂ are in each case H, or R₁ and R₂ are in each case methyl, or one of the substituents R₁ and R₂ is H and the other is methyl.

7. (Previously Presented) The oligonucleotide derivative according to claim 5, in which R₁ and R₂ are in each case methyl, or one of the substituents R₁ and R₂ is H and the other is methyl.

8. (Previously Presented) The oligonucleotide derivative according to claim 1, in which R₃ and R₄ are, independently of each other, H, -CH₃, -CH₂OH or -CH₂-O-CH₃.

9. (Previously Presented) The oligonucleotide derivate according to claim 1, in which n is 0.

10. (Currently Amended) The oligonucleotide derivative ~~according to claim 9~~, in which

n is 0,

A is a radical of the formula -C(H)(R₃)-N(R₁)(R₂), in which

R_3 is H, and R_1 and R_2 are defined as in claim 1.

11. (Cancelled).

12. (Cancelled).

13. (Cancelled).

14. (Cancelled).

15. (Previously Presented) The oligonucleotide derivate according to claim 1, in which V and W, as radicals of an internucleosidic bridging group, are, independently of each other, selected from the following group: 5'-O-P(O)(OH)-O-3' (phosphodiester), 5'-O-P(O)(SH)-O-3' (phosphorothioate), 5'-O-P(S)(SH)-O-3' (phosphodithioate), 5'-O-P(O)(CH₃)-O-3' (methylphosphonate), 5'-O-P(O)(NH-R₇)-O-3' (phosphoamidate) in which R₇ is C₁-C₃alkyl, 5'-O-P(O)(OR₈)-O-3' (phosphotriester) in which R₈ is C₁-C₃alkyl, 5'-O-S(O)₂-CH₂-3' (sulfonate), 5'-O-S(O)₂-NH-3' (sulfamate), 5'-NH-S(O)₂-CH₂-3' (sulfonamide), 5'-CH₂-S(O)₂-CH₂-3' (sulfone), 5'-O-S(O)-O-3' (sulfite), 5'-CH₂-S(O)-CH₂-3' (sulfoxide), 5'-CH₂-S-CH₂-3' (sulfide), 5'-O-CH₂-O-3' (formacetal), 5'-S-CH₂-O-3' (3'-thioformacetal), 5'-O-CH₂-S-3' (5'-thioformacetal), 5'-CH₂-CH₂-S-3' (thioether), 5'-CH₂-NH-O-3' (hydroxylamine), 5'-CH₂-N(CH₃)-O-3' (methylene(methylimino)), 5'-CH₂-O-N(CH₃)-3' (methyleneoxy(methylimino)), 5'-O-C(O)-NH-3' (5'-N-carbamate), 5'-CH₂-C(O)-NH-3' (amide), 5'-NH-C(O)-CH₂-3' (amide II), 5'-CH₂-NH-C(O)-3' (amide III) and 5'-C(O)-NH-CH₂-3' (amide IV), and the tautomeric forms thereof.

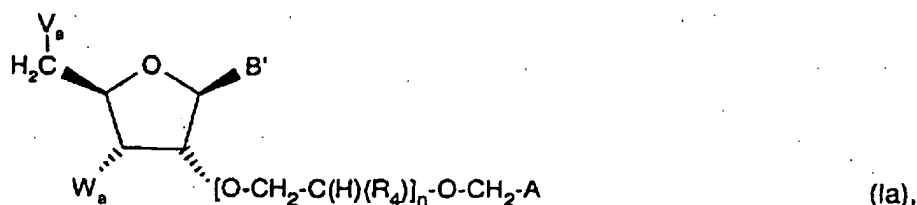
16. (Previously Presented) The oligonucleotide derivative according to claim 15, in which V and W, as radicals of an internucleosidic bridging group, are, independently of each other, selected from the following group: 5'-O-P(O)(OH)-O-3' (phosphodiester), 5'-O-P(O)(SH)-O-3' (phosphorothioate) and 5'-CH₂-C(O)-NH-3' (amide).

17. (Previously Presented) The oligonucleotide derivative according to claim 16, in which one of the radicals V or W, as radicals of an internucleosidic bridging group, is 5'-O-P(O)(OH)-O-3' (phosphodiester) and the other radical is 5'-O-P(O)(SH)-O-3' (phosphorothioate).

18. (Previously Presented) The oligonucleotide derivate according to claim 16, in which V and W as radicals of an internucleosidic bridging group, are in each case 5'-O-P(O)(OH)-O-3' (phosphodiester) or in each case 5'-O-P(O)(SH)-O-3' (phosphorothioate).

19. (Previously Presented) The oligonucleotide derivative according to claim 1, in which V and W, as terminal radicals, are, independently of each other, -OH, -NH₂ or a hydroxyl or amino group which is protected by a protecting group.

20. (Previously Presented) The oligonucleotide derivative according to claim 17, in which V, as terminal radical, is -OH, -NH₂ or a protected hydroxyl or amino group, and, W is -OH or -NH₂.
21. (Previously Presented) The oligonucleotide derivative according to claim 1, which has a length of from 3 to 50 nucleoside building blocks.
22. (Previously Presented) The oligonucleotide derivative according to claim 18, which has a length of from 10 to 25 nucleoside building blocks.
23. (Previously Presented) The oligonucleotide derivative according to claim 1, wherein the oligonucleotide derivative has a chimeric structure.
24. (Currently Amended) A compound of the formula (Ia)



in which

A is a radical of the formula -C(H)(R₃)-N(R₁)(R₂), in which

R₁ and R₂ are, independently of each other,

H,

C₁-C₁₀alkyl,

a radical of the formula II



in which each X is, in each case, independently of each other, a or N(R₆), R₅ and R₆ are,

in each case, independently of each other, H, C₁-C₁₀alkyl, amino-C₂-C₁₀alkyl, N-mono-

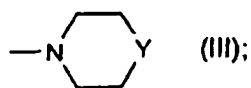
C₁-C₁₀alkylamino-C₂-C₁₀alkyl or N,N-di-C₁-C₁₀alkylamino-C₂-C₁₀alkyl, and m is an integer from 1 up to and including 3,

amino-C₃-C₁₀alkyl,

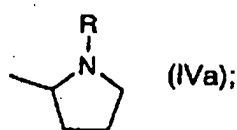
N-mono-C₁-C₁₀alkylamino-C₃-C₁₀alkyl, or

N,N-di-C₁-C₁₀alkylamino-C₃-C₁₀alkyl; or in which

-N(R₁)(R₂) are together a radical of the formula (III)



in which Y is O, S, SO, SO₂ or N(R₇), and R₇ is H or -CH₃;
 R₃ is H, -CH₃, -CH₂CH₃, -CH₂OH or -CH₂-O-C₁-C₄alkyl; or
 A is a radical of the formula (IVa) or (IVb)



in which R, independently, has the meaning of R₁ or R₂, and U is O or CH₂;

R₄ is H, -CH₃, -CH₂CH₃, -CH₂OH or -CH₂-O-C₁-C₄alkyl;

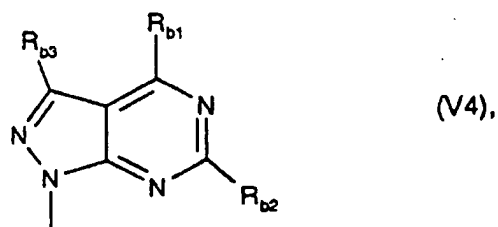
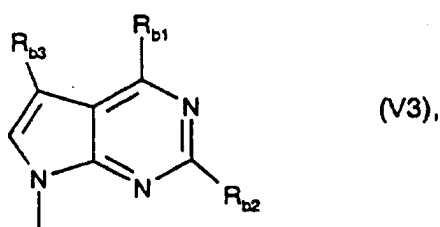
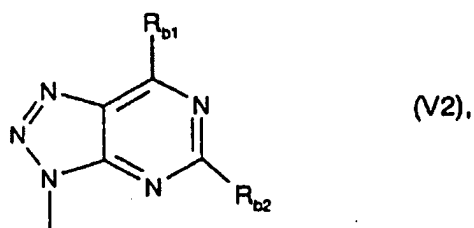
n is 0, 1 or 2;

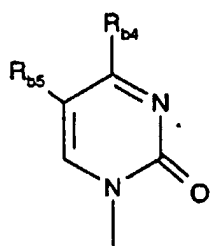
B' is the radical of a protected or unprotected nucleic acid base; and

V_a and W_a are, independently of each other, -OH, -NH₂ or identically or differently protected hydroxyl or amino groups,

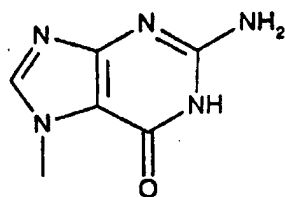
where those compounds are excepted in which, in the radical A, two heteroatoms are linked to the same carbon atom,

and where other reactive groups are present in the protected or unprotected state state, and
wherein B is a radical of any of the formulas (V2) to (V14):

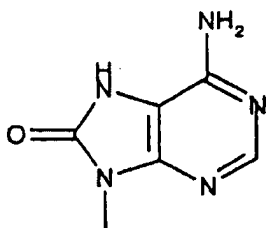




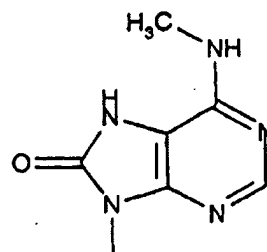
(V5),



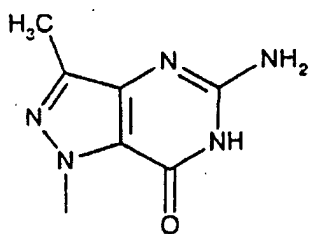
(V6),



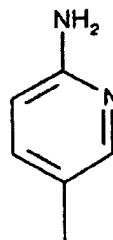
(V7),



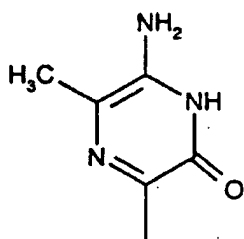
(V8),



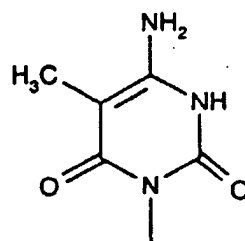
(V9),



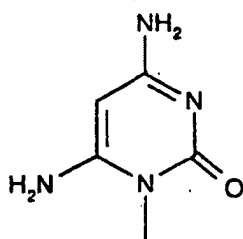
(V10),



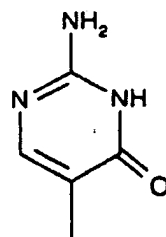
(V11),



(V12),



(V13),



(V14)

in which

R_{b1} is $-NH_2$, $-SH$ or $-OH$;

R_{b2} is H , $-NH_2$ or $-OH$; and

R_{b3} is H , Br , I , $-CN$, $-C\equiv C-CH_3$, $-C(O)NH_2$ or $-CH_3$;

R_{b4} is -NH₂ or -OH; and

R_{b5} is H, F, Br, I, -CN, -C≡C-CH₃, -C(O)NH₂ or -CH₃.

25. (Previously Presented) The compound according to claim 24, in which

A is a radical of the formula -C(H)(R₃)-N(R₁)(R₂), in which

R₁ and R₂ are, independently of each other, H, C₁-C₅alkyl, amino-C₂-C₅alkyl, N-Mono-C₁-C₃alkylamino-C₂-C₅alkyl, N,N-di-C₁-C₃alkylamino-C₂-C₅alkyl or a radical of the formula II



in which X is O or N(R₆), R₅ and R₆ are, independently of each other, H, C₁-C₃alkyl, amino-C₂-C₃alkyl, N-mono-C₁-C₃alkylamino-C₂-C₅alkyl or N,N-di-C₁-C₃alkylamino-C₂-C₅alkyl, and m is 1.

26. (Previously Presented) The compound according to claim 25, in which

R₁ and R₂ are, independently of each other, H, methyl, ethyl, aminoethyl, aminopropyl, N-monomethylaminoethyl, N-monomethylaminopropyl, N-monoethylaminoethyl, N-monoethylaminopropyl, N,N-dimethylaminoethyl, N,N-dimethylaminopropyl, N,N-diethylaminoethyl, N,N-diethylaminopropyl, or a radical of the formula II



in which X is O or N(R₆), R₅ and R₆ are, independently of each other, H, methyl, ethyl or propyl and m is 1.

27. (Previously Presented) The compound according to claim 26, in which

R₁ and R₂ are, independently of each other, H, methyl, ethyl, aminoethyl, N-monomethylaminoethyl, N-monoethylaminoethyl, N,N-dimethylaminoethyl or N,N-diethylaminoethyl.

28. (Previously Presented) The compound according to claim 27, in which

R₁ and R₂ are, independently of each other, H, methyl or ethyl.

29. (Previously Presented) The compound according to claim 28, in which

R₁ and R₂ are in each case H, or

R₁ and R₂ are in each case methyl, or

one of the substituents R₁ and R₂ is H and the other is methyl.

30. (Previously Presented) The compound according to claim 29, in which

R₁ and R₂ are in each case methyl, or

one of the substituents R₁ and R₂ is H and the other is methyl.

31. (Previously Presented) The compound according to claim 24, in which R_3 and R_4 are, independently of each other, H, $-\text{CH}_3$, $-\text{CH}_2\text{OH}$ or $-\text{CH}_2\text{-O-CH}_3$.

32. (Previously Presented) The compound according to claim 24, in which n is 0.

33. (Currently Amended) The compound according to claim ~~32~~, 24, in which n is 0.

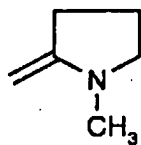
A is a radical of the formula $-\text{C}(\text{H})(\text{R}_3)-\text{N}(\text{R}_1)(\text{R}_2)$, in which R_3 is H, and R_1 and R_2 are defined as in claim 24.

34. (Cancelled).

35. (Cancelled).

36. (Cancelled).

37. (Previously Presented) The compound according to claim 24, in which the protecting group for exocyclic amino groups of the nucleic acid base B' is selected from the following group: $-\text{C}(\text{O})\text{CH}_3$, $-\text{C}(\text{O})-\text{CH}(\text{CH}_3)_2$, $-\text{C}(\text{O})$ -phenyl, $-\text{C}(\text{O})-\text{CH}_2\text{-O-phenyl}$, $-\text{C}(\text{O})-\text{CH-p}(\text{tert-butyl})\text{phenyl}$, $-\text{C}(\text{O})-\text{CH}_2\text{-O-p}(\text{tert-butyl})\text{phenyl}$, $-\text{C}(\text{O})-\text{CH}_2\text{-O-p}(\text{isopropyl})\text{phenyl}$, $=\text{CH-N}(\text{CH}_3)_2$,

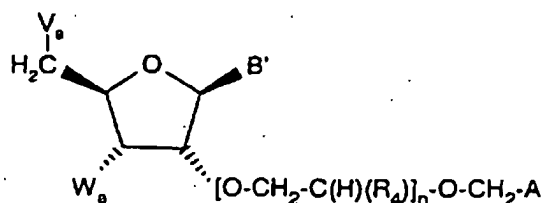


$=\text{CH-N}(\text{butyl})_2$ and

38. (Previously Presented) The compound according to claim 24, in which the protecting group for V_a or W_a , as a protected hydroxyl or amino group, is a trityl-type protecting group.

39. (Previously Presented) The compound according to claim 38, wherein the trityl-type protecting group is selected from the following group: trityl, 4-monomethoxytrityl, 4,4'-dimethoxytrityl and 4,4',4''-tris-tert-butyltrityl.

40. (Previously Presented) A process for preparing the compound of the formula (Ia) according to claim 24



(Ia),

in which V_a , W_a , A and B' are defined as in claim 24, and

(a) n is 0 and R_4 is therefore absent,
which comprises reacting a compound of the formula (A)



in which V_a and W_a are, independently of each other, a protected hydroxyl or amino group, and B' is defined as above, with exocyclic amino groups in B' being protected by protecting groups, with a compound of the formula (B)

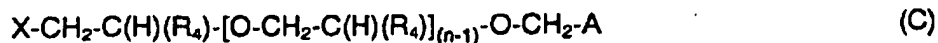


in which X is Cl, Br, I, tosyl-O or mesyl-O, and A is defined as above, with primary and secondary amino groups and primary hydroxyl groups in A being protected by protecting groups; or

(b) R_4 is H, $-CH_3$, $-CH_2CH_3$, $-CH_2OH$ or $-CH_2-O-C_1-C_4$ alkyl and n is 1 or 2,
which process comprises reacting a compound of the formula (A)

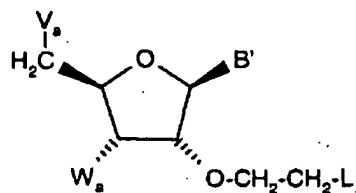


in which V_a and W_a are, independently of each other, a protected hydroxyl or amino group, and B is defined as above, with exocyclic amino groups in B' being protected by the protecting groups, with a compound of the formula (C)



in which X is Cl, Sr, I, tosyl-O or mesyl-O, and R_4 and A are defined as above, with primary and secondary amino groups and primary hydroxyl groups in A being protected by protecting groups; or

(c) R_4 is H and n is 1 or 2,
which process comprises reacting a compound of the formula (D)



(D),

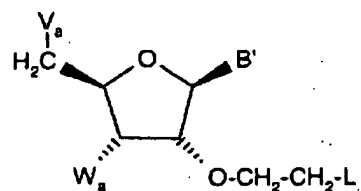
in which V_a and W_a are, independently of each other, a protected hydroxyl or amino group, B' is defined as above, with exocyclic amino groups in B' being protected by protecting groups, and L is a leaving group,

with a compound of the formula (E)



in which A is defined as above, and with primary and secondary amino groups and primary hydroxyl groups in A being protected by protecting groups; or

(d) n is 0 and R_4 is therefore absent, and A is a radical of the formula $-\text{C}(\text{H})(\text{R}_3)-\text{N}(\text{R}_1)(\text{R}_2)$, which process comprises reacting a compound of the formula (D)



(D),

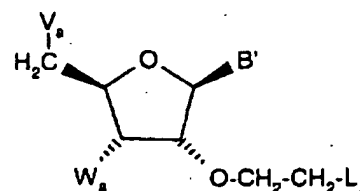
which is defined as above,

with a compound of the formula (F)



in which R_1 , R_2 or the group $-\text{N}(\text{R}_1)(\text{R}_2)$ are defined as in Claim 24, and with functional groups in R_1 or R_2 being protected if necessary; or

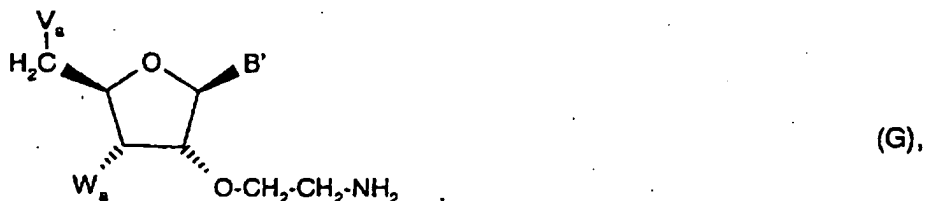
(e) n is 0 and R_4 is therefore absent and A is a radical of the formula $-\text{C}(\text{H})(\text{R}_3)-\text{N}(\text{R}_1)(\text{R}_2)$, which process comprises reacting a compound of the formula (D)



(D),

which is defined as above,

with an azide and subsequent reduction, if necessary using a catalyst, to give a compound of the formula (G)



and, optionally, subjecting the compound of the formula (G) to further derivatization; within cases (a) to (e), protected groups subsequently being de-protected if necessary.

41. (Currently Amended) A process for preparing the oligonucleotide derivative according to claim 4, 24,

the process comprising the following steps:

(i) converting a compound of the formula (Ia) according to claim 24 into a form suitable for oligonucleotide synthesis,

(ii) using the compound of the formula Ia according to claim 24, which compound is in a suitable form, in the oligonucleotide synthesis.

42. (Previously Presented) A method for producing an oligonucleotide, the method comprising the step of providing at least one compound of the formula (Ia) according to claim 24 in a form suitable as a nucleoside building block and joining the at least one compound in a sequence with one or more other nucleoside building blocks, such that the compounds of formula (Ia) are distributed randomly in the sequence.

43. (Previously Presented) The method of claim 42, wherein the oligonucleotide comprises an antisense oligonucleotide.

44. (Previously Presented) The oligonucleotide derivative according to claim 12, wherein the oligonucleotide derivative comprises an antisense oligonucleotide.

45. (Previously Presented) The oligonucleotide derivative according to claim 1, wherein the oligonucleotide derivative is a triplex-forming oligonucleotide.

46. (Currently Amended) The oligonucleotide derivative according to claim ~~45~~, 1, wherein the oligonucleotide derivative is ~~as defined in claim 11~~ a triplex-forming oligonucleotide.

47. (Currently Amended) The oligonucleotide derivative according to claim 45, wherein ~~the oligonucleotide derivative is as defined in claim 12~~

B is (V2), (V3), (V4), or (V5), in which

R_{b1} is -NH₂, -SH or -OH;

R_{b2} is H, -NH₂ or -OH; and

R_{b3} is H, Br, I, -CN, -C≡C-CH₃, -C(O)NH₂ or -CH₃;

R_{b4} is -NH₂ or -OH; and

R_{b5} is H, F, Br, I, -CN, -C≡C-CH₃, -C(O)NH₂ or -CH₃.

48. (Currently Amended) A pharmaceutical composition, which comprises an oligonucleotide derivative according to claim 1, or a pharmaceutically tolerated salt thereof, in a pharmaceutically effective quantity, ~~if desired~~ optionally together with a pharmaceutically tolerated excipient and/or auxiliary substance.

49. (Previously Presented) The pharmaceutical composition according to claim 48, which additionally comprises a customary cytostatic agent.

50. (Original) An oligonucleotide derivative according to claim 1, or a pharmaceutically tolerated salt thereof, for use in the therapeutic treatment of a mammalian subject, including man.

51. (Previously Presented) A process for preparing a composition, the process comprising the step of providing an oligonucleotide derivative according to claim 1 or a pharmaceutically acceptable salt thereof.

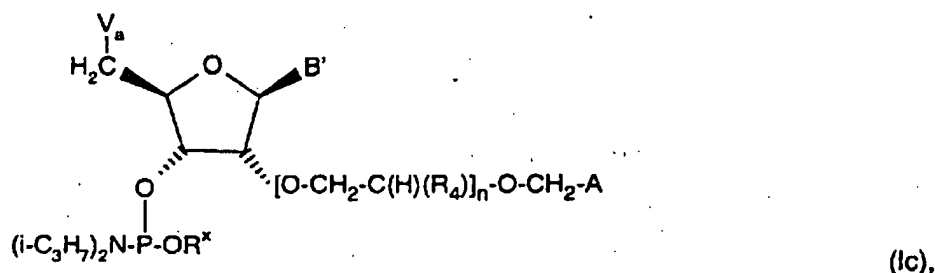
52. (Original) A process for the therapeutic treatment of a pathological state, in a mammalian subject including man, which is characterized by the expression of a protein or an RNA molecule, which comprises administering a pharmaceutical composition according to claim 48 to the mammalian subject.

53. (Currently Amended) A process for modulating the expression of a protein or an RNA molecule in a cell, which comprises bringing the cell, or a tissue or body fluid containing this cell, into contact with an oligonucleotide derivative according to claim 1 or a pharmaceutical composition ~~according to claim 48 which comprises an oligonucleotide derivative according to claim 1, or a pharmaceutically tolerated salt thereof, in a pharmaceutically effective quantity,~~ optionally together with a pharmaceutically tolerated excipient and/or auxiliary substance.

54. (Previously Presented) A probe comprising the oligonucleotide derivative according to claim 1.

55. (Previously Presented) A therapeutic treatment of a mammalian subject, comprising the step of administering a composition comprising the compound of the formula (Ia) according to claim 24.

56. (Original) A compound of the formula (Ic)



in which V_a , R_4 , A and B' are defined as in claim 24, and R^x is a protecting group.

57. (Original) An oligonucleotide derivative according to claim 1, wherein the oligonucleotide derivative is essentially complementary to the region which extends from base position 2484 to base position 2503 of human c-ras mRNA.

58. (Currently Amended) An oligonucleotide derivative according to claim 57, wherein the oligonucleotide derivative possesses a base sequence according to SEQ ID NO: 2
~~SEQ ID NO: 2 or a base sequence which is analogous thereto.~~

59. (Cancelled).

60. (Cancelled).

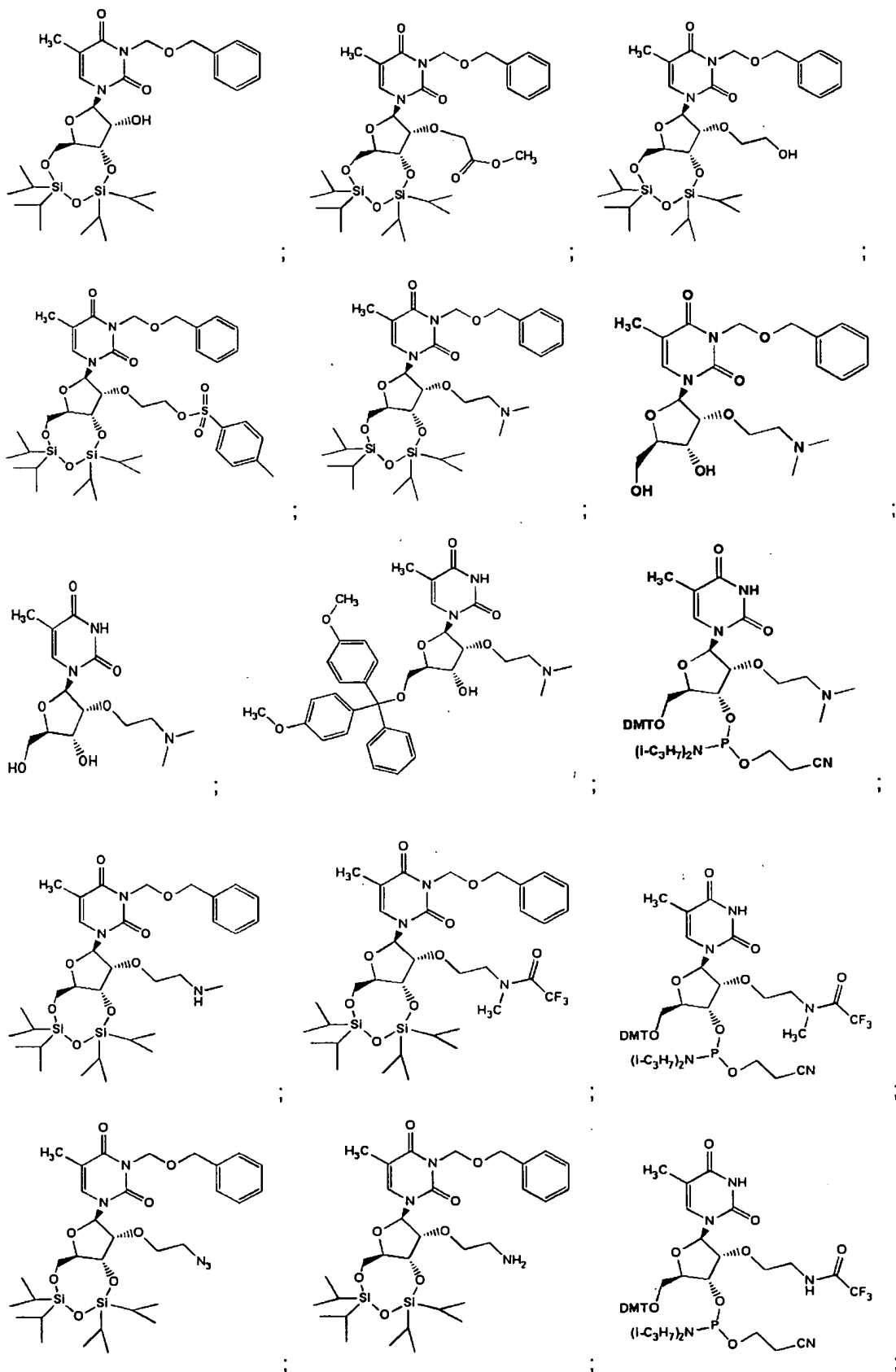
61. (Not Entered).

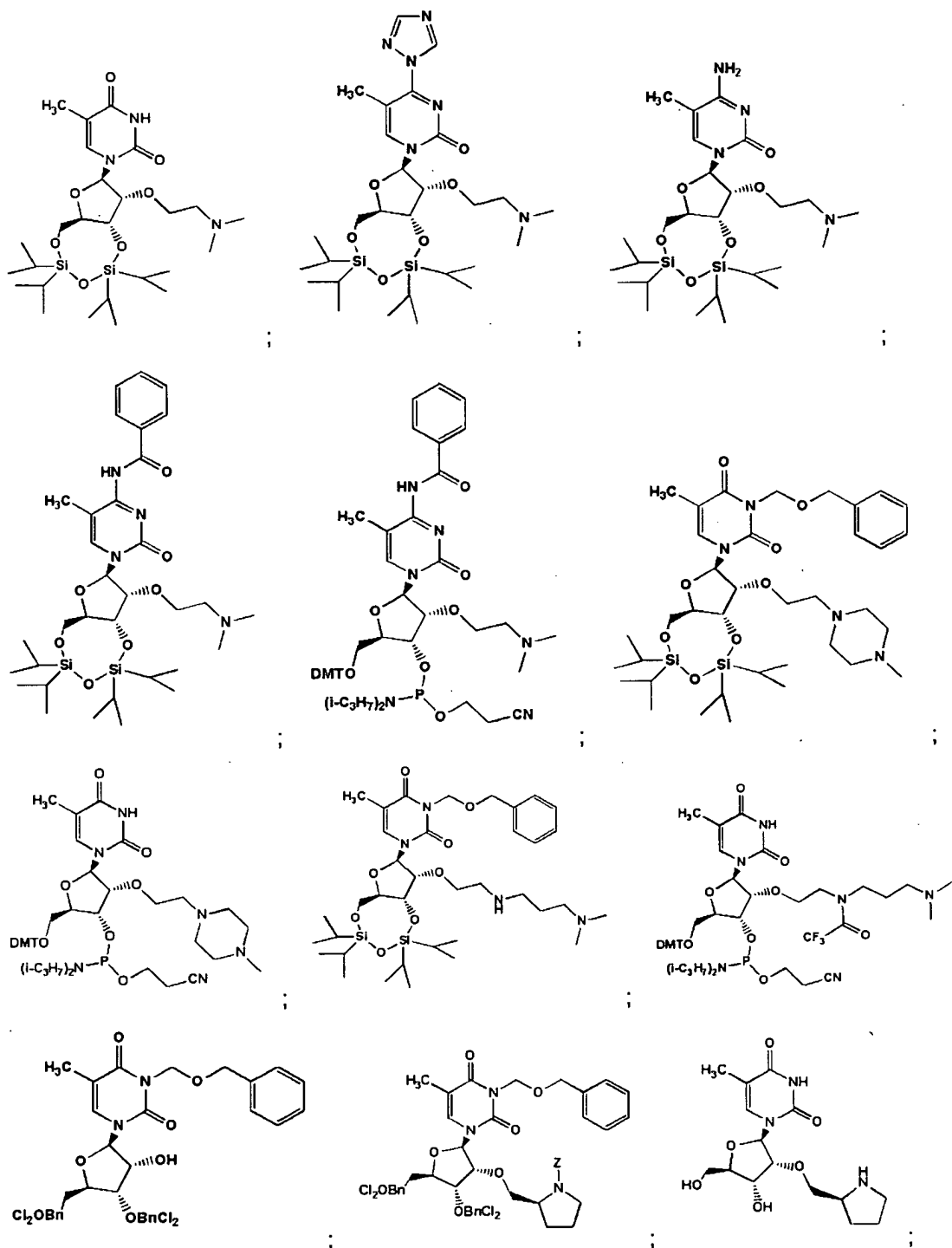
62. (Not Entered).

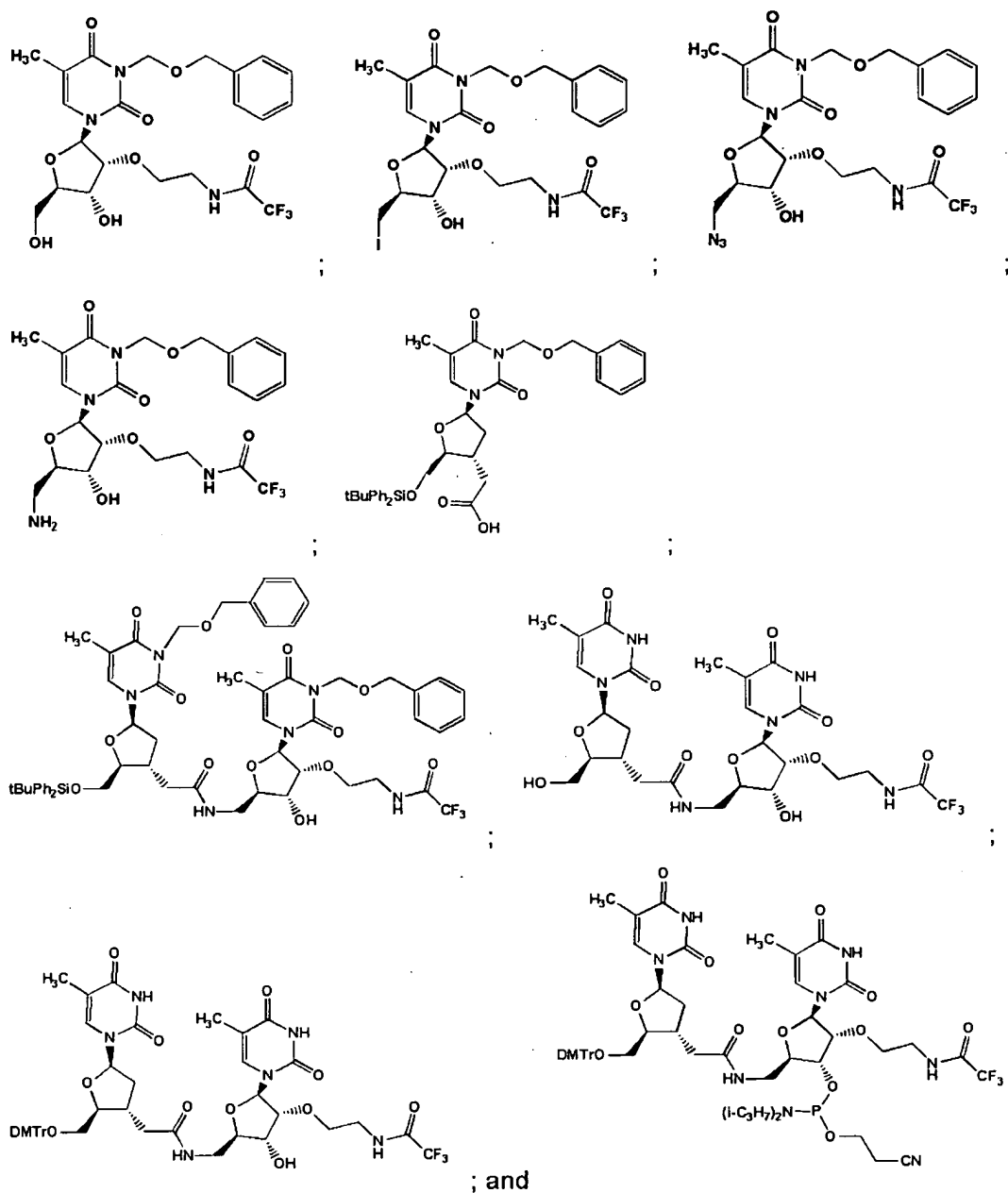
63. (New) The oligonucleotide derivative of claim 11, wherein B is a radical of any of the formulas of (V2) to (V14).

64. (New) The oligonucleotide derivative of claim 34, wherein B is a radical of any of the formulas of (V2) to (V14).

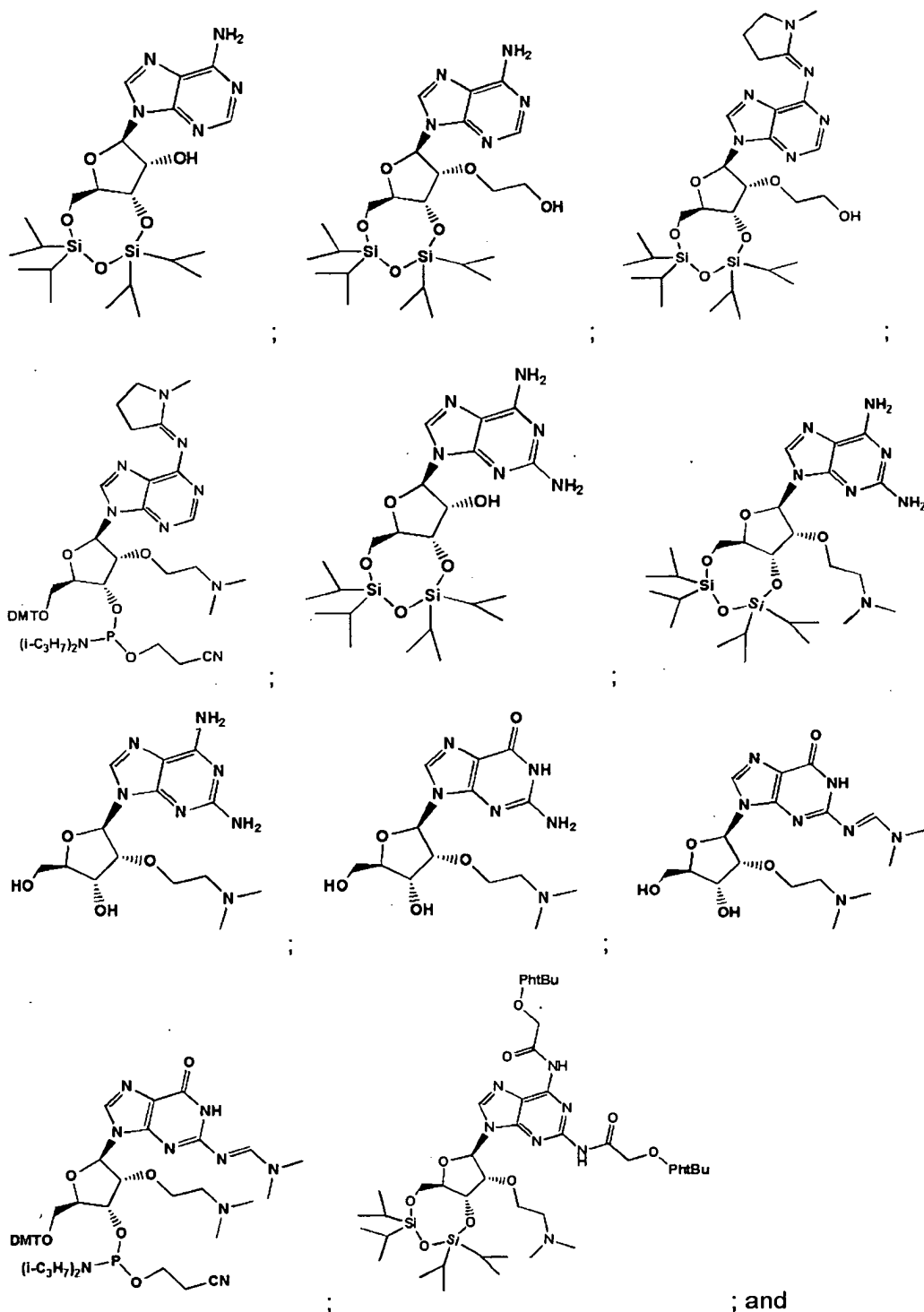
65. (New) A compound selected from:







66. (New) A compound selected from:



; and

